

## WHAT IS CLAIMED IS:

1. A recombinant viral vector comprising an adenoviral nucleic acid backbone, wherein said nucleic acid backbone comprises in sequential order: a left ITR, a termination signal sequence, an E2F responsive promoter which is operably linked to a gene essential for replication of the recombinant viral vector, an adenoviral packaging signal, and a right ITR.
2. The recombinant viral vector of claim 1, wherein the termination signal sequence is the SV40 early polyadenylation signal sequence.
3. The recombinant viral vector of claim 1, wherein the E2F responsive promoter is the human E2F-1 promoter.
4. The recombinant viral vector of claim 1, wherein the adenoviral nucleic acid backbone is derived from adenovirus serotype 5 (Ad5) or serotype 35 (Ad35).
5. The recombinant viral vector of claim 1, wherein the gene essential for replication is the E1A gene.
6. The recombinant viral vector of claim 1, further comprising a deletion upstream of the termination signal sequence.
7. The recombinant viral vector of claim 6, further comprising a deletion between nucleotides 103 and 551 of the adenoviral type 5 backbone or other corresponding bps of other Adenovirus serotypes.
8. The recombinant viral vector of claim 1, further comprising a mutation or deletion in the E3 region.
9. The recombinant viral vector of claim 5, further comprising a tissue-specific promoter operably linked to E4.
10. The recombinant viral vector of claim 9, wherein said tissue-specific promoter is derived from the human telomerase reverse transcriptase promoter.
11. The recombinant viral vector of claim 9, wherein said tissue-specific promoter is the Trtex promoter SEQ ID NO:94 or the TERT promoter of SEQ ID NO:93.
12. The recombinant viral vector of claim 9, which is the Ar17pAE2fFTrtex vector.
13. The recombinant viral vector of claim 9, wherein said tissue-specific promoter is derived from the osteocalcin promoter.

202206091801

14. The recombinant viral vector of claim 8, wherein the E3 region has been deleted from said backbone.
15. The recombinant viral vector of claim 1, which is the Ar6pAE2fF vector, or the Ar35E2FE1a vector.
16. The recombinant viral vector of claim 1, further comprising a mutation or deletion in the E1b gene.
17. The recombinant viral vector of claim 16, wherein said mutation or deletion results in the loss of the active 19kD protein expressed by the wild-type E1b gene.
18. The recombinant viral vector of claim 1, further comprising a therapeutic gene.
19. The recombinant viral vector of claim 18, wherein said therapeutic gene is inserted in the E3 region.
20. The recombinant viral vector of claim 19, wherein said therapeutic gene is inserted in place of the 19kD or 14.7 kD E3 gene.
21. The recombinant viral vector of claim 18, wherein said therapeutic gene is an immunostimulatory gene.
22. The recombinant viral vector of claim 21, wherein said immunostimulatory gene is a cytokine.
23. The recombinant viral vector of claim 21, wherein the immunostimulatory gene is selected from the group consisting of GM-CSF, IL1, IL2, IL4, IL5, IFN $\alpha$ , IFN $\gamma$ , TNF $\alpha$ , IL12, IL18, and flt3.
24. The recombinant viral vector of claim 21, wherein said immunostimulatory gene is selected from the group consisting of MIP1 $\alpha$ , MIP3 $\alpha$ , CCR7 ligand, calreticulin, B7, CD28, MHC class I, MHC class II, and TAPs.
25. The recombinant viral vector of claim 21, wherein said immunostimulatory gene is a tumor associated antigen.
26. The recombinant viral vector of claim 25, wherein said tumor associated antigen is selected from the group consisting of MART-1, gp100(pmel-17), tyrosinase, tyrosinase-related protein 1, tyrosinase-related protein 2, a melanocyte-stimulating hormone receptor, MAGE1, MAGE 2, MAGE 3, MAGE 12, BAGE, GAGE, NY-ESO-1,  $\beta$ -catenin, MUM-1, CDK-4, caspase 8,

KIA 0205, HLA-A2R1701,  $\alpha$ -fetoprotein, telomerase catalytic protein, G-250, MUC-1, carcinoembryonic protein, p53, Her2/neu, triosephosphate isomerase, CDC-27, and LDLR-FUT.

27. The recombinant viral vector of claim 21, wherein said immunostimulatory gene is an antibody that blocks inhibitory signals.

28. The recombinant viral vector of claim 27, wherein the inhibitory signal is due to expression of CTLA4.

29. The recombinant viral vector of claim 18, wherein the therapeutic gene is an anti-angiogenic gene.

30. The recombinant viral vector of claim 29, wherein said anti-angiogenic gene is selected from the group consisting of a VEGF/VEGFR antagonist, an angiopoietin/Tie antagonist, an Ephrin/Eph antagonist, and an FGF/FGFR antagonist.

31. The recombinant viral vector of claim 29, wherein said anti-angiogenic gene is an inhibitor of PDGF, TGF $\beta$ , or IGF-1.

32. The recombinant viral vector of claim 29, wherein said anti-angiogenic gene is a fragment of an extracellular matrix protein.

33. The recombinant viral vector of claim 32, wherein said extracellular matrix protein is selected from the group consisting of angiostatin, endostatin, kininostatin, fibrinogen-E, thrombospondin, tumstatin, canstatin, and restin.

34. The recombinant viral vector of claim 29, wherein the anti-angiogenic gene is a fragment of TrpRS.

35. The recombinant viral vector of claim 29, wherein the anti-angiogenic gene is selected from the group consisting of sFlt-1, sFlk, sNRP1, sTie-2, IP-10, PF-4, Gro-beta, IFN-gamma (Mig), sEphB4, sephrinB2, vasostatin, PEDF, prolactin fragment, proliferin-related protein, METH-1, and METH-2.

36. The recombinant viral vector of claim 18, wherein said therapeutic gene is a suicide gene.

37. The recombinant viral vector of claim 36, wherein said suicide gene is selected from the group consisting of CPG2, CA, CD, cyt-450, dCK, HSV-TK, NR, PNP, TP, VZV-TK, and XGPRT.

10081969 "022202"

38. The recombinant viral vector of claim 1, wherein said recombinant viral vector is capable of selectively replicating in and lysing Rb-pathway defective cells.
39. The recombinant viral vector of claim 38, wherein tumor-selectivity is at least about 3-fold as measured by E1A RNA levels in infected tumor vs. non-tumor cells.
40. A recombinant viral vector comprising an Ad5 nucleic acid backbone, wherein said backbone comprises in sequential order: a left ITR, an SV40 early polyA site, a human E2F-1 promoter operably linked to the E1A gene, an adenoviral packaging signal, and a right ITR.
41. The recombinant viral vector of claim 40 further comprising a deletion between nucleotides 103 and 551 of the adenoviral backbone.
42. The recombinant viral vector of claim 40 further comprising a mutation or deletion in the E1b gene, wherein said mutation or deletion results in the loss of the active 19kD protein expressed by the wild-type E1b gene.
43. The recombinant viral vector of claim 40, further comprising a tissue-specific promoter operably linked to E4.
44. The recombinant viral vector of claim 43, wherein said tissue-specific promoter is derived from the human telomerase reverse transcriptase promoter.
45. The recombinant viral vector of claim 43, wherein said tissue-specific promoter is the Trtex promoter.
46. The recombinant viral vector of claim 43, which is the Ar17pAE2fTrtex vector.
47. The recombinant viral vector of claim 43, wherein said tissue-specific promoter is derived from the osteocalcin promoter.
48. An adenoviral vector particle comprising the viral vector of claims 1.
49. The adenoviral vector particle of claim 48, further comprising a targeting ligand included in a capsid protein of said particle.
50. The particle of claim 49, wherein said capsid protein is a fiber protein.
51. The particle of claim 50, wherein said ligand is in the HI loop of said fiber protein.
52. A method of selectively killing a neoplastic cell in a cell population which comprises contacting an effective amount of the adenoviral vector particle of claim 48 with said cell

population under conditions where the recombinant viral vector can transduce the cells of said cell population.

53. The method of claim 52, wherein the neoplastic cell has a defect in the Rb-pathway.
54. A pharmaceutical composition comprising the adenoviral vector particle of claim 48 and a pharmaceutically acceptable carrier.
55. A method of treating a host organism having a neoplastic condition, comprising administering a therapeutically effective amount of the composition of claim 54 to said host organism.
56. The method of treatment of claim 55, wherein the host organism is a human patient.
57. The method of treatment of claim 55, wherein the neoplastic condition is lung, breast, prostate, or colon cancer.
58. The vector of claim 1, wherein said backbone comprises a gene of the E3 coding region.
59. The vector of claim 58, wherein said gene is selected from the group consisting of E3-6.7, KDa, gp19KDa, 11.6KDa (ADP), 10.4 KDa (RID $\alpha$ ), 14.5 KDa (RID $\beta$ ), and E3-14.7Kda.
60. The method of treatment of claim 55, wherein administration is the intratumoral injection of a therapeutically effective dosage of the composition of claim 54.